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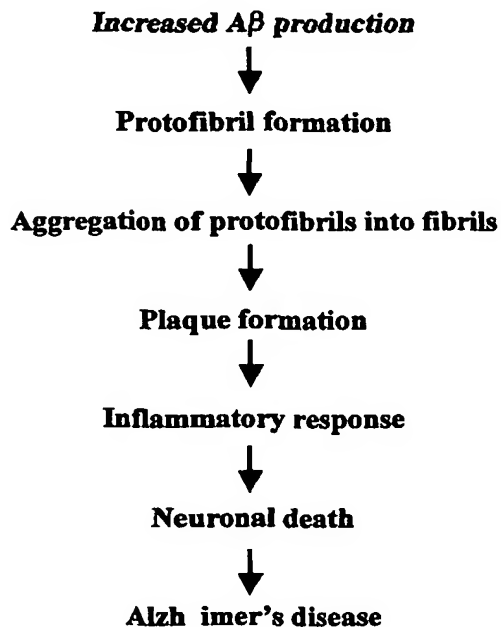
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(54) Title: METHODS FOR THE IDENTIFICATION OF AGENTS THAT MODULATE THE STRUCTURE AND PROCESSING OF BETA-AMYLOID PRECURSOR PROTEIN

The amyloid cascade leading to Alzheimer's disease



(57) Abstract: The present invention provides methods for the screening and identification of agents from a large library of molecular structures that can alter the cleavage of amyloid precursor protein (AP). Agents identified by the methods of the present invention that modify the cleavage of APP can be used in the treatment and prevention of Alzheimer's disease. The methods select for and identify effector agents that bind to APP causing a structural change in the structure of APP in such a way that the efficiency of the cleavage of a secretase is modulated. Further, the methods are carried out in an in vivo system that provides for physiological conditions similar or identical to conditions for APP processing. Agents can be selected for their ability to cause a decrease in the amount of β -secretase or γ -secretase cleavage of APP, or for an increase in α -secretase cleavage of APP. The agents can be, particularly peptide agents, can be converted into a peptidomimetic, an isosteric replacement compound, a D-amino acid analog, or non-peptidyl compound for treating Alzheimer's disease or any other amyloid related or prion related disease. The agents or derivatives thereof can be formulated for intravenous, parenteral, topical, sustained release, intranasal, or inhalation use.

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